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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/551,396

10/19/2006

Peter John Meikle

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EXAMINER

COUNTS, GARY W

ART UNIT

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/551,396	<b>Applicant(s)</b> MEIKLE ET AL.	
	<b>Examiner</b> GARY W. COUNTS	<b>Art Unit</b> 1641	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 27 January 2011.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-42,46,51-53 and 56-74 is/are pending in the application.
- 4a) Of the above claim(s) 1-41 and 58-73 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 42,46,51-53,56,57 and 74 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>11/23/10</u> .  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 01/27/11 has been entered.

Currently, claims 1-42, 46, 51-53, and 56-74 are pending. Claims 1-41 and 58-73 are withdrawn as being directed to non-elected inventions. Claims 42, 46, 51-53, 56, 57 and 74 are under examination.

### **Withdrawn Rejections**

All rejections of claims not reiterated herein, have been withdrawn.

### ***Claim Objections***

2. Claim 46 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 46 recites "wherein the sample is selected from dried blood or plasma". This recitation fails to further limit

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claim 42 because claim 42 already requires that the sample is either dried blood or plasma.

***Claim Rejections - 35 USC § 112***

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 42, 46, 51-53, 56, 57 and 74 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims recite “and a significant deviation of any of the adjusted target quantities compared to the adjusted reference quantities is a pre-clinical or clinical indication of a specific LSD, wherein a deviation is significant if the absolute value of the deviation is greater than or equal to a standard deviation calculated by a Mann-Whitney U (MWU) test”. The specification on page 5, paragraph 0011 discloses that the ability to identify specific LSD enzymes in an automated multiplex assay will have a significant impact. The specification on page 33, paragraph 0105 discloses that figure 25 shows the Pearson correlation coefficient between each pair of target protein analytes. With the exception of A-iduronidase, the target antigens showed a significant correlation to the other antigens. The specification on pages 10-11, paragraph 0048 discloses that

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the pre-clinical status or the clinical status of an LSD can then be determined by comparing a deviation of the adjusted target quantity to the adjusted reference quantity. The specification on page 30, paragraph 0096 discloses that in contrast to absolute marker measurements, the multiplex allows each protein to be compared using ratios. For example, there was one four month old Pompe patient who had A-glucosidase blood spots levels in the lower range of the control group, this patient would have been missed in a typical screening program if the determined cut-offs used only absolute protein levels. There is no description in the specification disclosing a significant deviation of the adjusted target quantity compared to the adjusted reference quantity is a pre-clinical or clinical indication of a specific LSD, wherein a deviation is significant if the absolute value of the deviation is greater than or equal to a standard deviation calculated by a Mann-Whitney U (MWU) test. Furthermore, none of the originally filed claims recited the limitations in question. Recitation of claim limitations lacking literal or adequate descriptive support in the specification or originally filed claims constitutes new matter.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 42, 46, 51-53, 56, 57 and 74 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 42 step (g) is vague and indefinite because it is unclear how the first and second fluorophores are related to detection in the instantly recited claim. Also, the instant claims require the detection of multiple targets and it is unclear how one microsphere comprising only one antibody for a specific target is also able to detect the other targets in the assay. Is there more than one type of microsphere or more than one type of antibody? See also deficiency found in claim 74. Therefore, it is unclear how the determination of the targets is made in the instantly recited claim.

### ***Response to Arguments***

Applicant's arguments filed 01/27/11 have been fully considered but they are not persuasive.

#### 112 first new matter

Applicant argues that the term “and a significant deviation of any of the adjusted target quantities compared to the adjusted reference quantities is a pre-clinical or clinical indication of a specific LSD, wherein a deviation is significant if the absolute value of the deviation is greater than or equal to a standard deviation calculated by a Mann-Whitney U (MWU) test” is supported by the specification and does not constitute new matter. The Applicant states that Example 3 describes, a multiplex conducted using A-iduronidase, a-glucosidase, LAMP-1 and saposin ., Applicant states that paragraph 0097 describes the improved accuracy obtained by calculating ratios of a-glucosidase to LAMP-1, and a-iduronidase to LAMP-. And that paragraph 0095 shows

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that MWU test values were used to determine significance in deviations from control values.

This argument is not found persuasive because of reasons stated above and in the previous office actions. Further, after reviewing paragraphs 0095 and 0097 of the specification the disclosure does not describe a significant deviation of the adjusted target quantity compared to the adjusted reference quantity is a pre-clinical or clinical indication of a specific LSD, wherein a deviation is significant if the absolute value of the deviation is greater than or equal to a standard deviation calculated by a Mann-Whitney U (MWU) test. Nowhere in the specification does is disclose a significant deviation of the adjusted target quantity compared to the adjusted reference quantity is a pre-clinical or clinical indication of a specific LSD, wherein a deviation is significant if the absolute value of the deviation is greater than or equal to a standard deviation calculated by a Mann-Whitney U (MWU) test.

112 2<sup>nd</sup> rejection:

Applicant argues that that the specification describes how the first and second fluorophores are related to detection. Applicant states that this is shown in Figure 10, and described in paragraphs [0074] and [0089] of the specification.

This argument is not found persuasive because although the claims are read in light of the specification, limitations from the specification are not read into the claims and the claims must stand on their own merits. Therefore, the claims as currently recited do not make clear how the first and second fluorophores are related to detection. Also, the instant claims require the detection of multiple targets and it is unclear how

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one microsphere comprising only one antibody for a specific target is also able to detect the other targets in the assay. Is there more than one type of microsphere or more than one type of antibody?

Applicant argues that in the currently disclosed assay, each microsphere is labeled internally with a fixed ratio of two different fluorophores, which combine to generate a detectable fluorescent signal and that this allows for creation of microspheres having a multitude of detection signals by creating microspheres with varying ratios of the two fluorophores.

This argument is not found persuasive because of reasons stated above that limitations from the specification are not read into the claim. Further, as stated above and previous it is unclear how only one microsphere comprising only one antibody for a specific target as currently recited detects or is capable of detecting multiple targets in the sample.

### ***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GARY W. COUNTS whose telephone number is (571)272-0817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on (571) 272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/ Gary W. Counts/  
Examiner, Art Unit 1641

/Melanie J. Yu/  
Primary Examiner, Art Unit 1641